

CLAIMS

1. A method of treating or preventing hot flashes in a patient comprising administering to the patient in need of such treatment or prevention a therapeutically effective amount of a prodrug of a GABA analog, or a pharmaceutically acceptable salt, hydrate or solvate thereof.
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2. A method of treating or preventing hot flashes in a patient comprising administering to the patient in need of such treatment or prevention a pharmaceutical composition comprising a therapeutically effective amount of a prodrug of a GABA analog, or a pharmaceutically acceptable salt, hydrate or solvate thereof and a pharmaceutically acceptable vehicle.
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3. The method of Claim 1 or Claim 2, wherein the GABA analog is gabapentin or pregabalin.
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4. The method of Claim 3, wherein the GABA analog is administered in an amount of between about 10 mg to about 5000 mg per day.
- 20 5. The method of Claim 1, wherein the patient is a female patient.
6. The method of Claim 5, wherein the female patient is postmenopausal.
7. The method of Claim 6, wherein menopause is drug induced or surgically induced.
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8. The method of Claim 1, wherein the patient is a male patient.
9. The method of Claim 5 or Claim 8, wherein the hot flashes are drug-induced.
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10. The method of Claim 1 or Claim 2, wherein the prodrug is administered orally, parenterally, subcutaneously, intravenously, intramuscularly, intraperitoneally, intranasally instillationally, intracavitarally or intravesical

instillationally, intraocularly, intraarterially, intralesionally, by implantation or by application to mucous membranes.

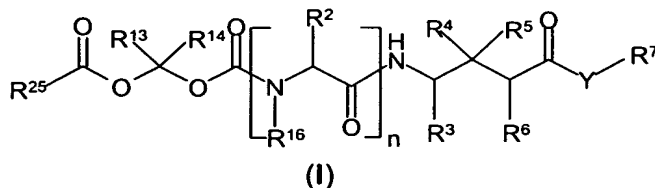
11. The method of Claim 1 or Claim 2, wherein the prodrug is
5 administered orally.

12. The method of Claim 1 or Claim 2, comprising administering the prodrug in a sustained release oral dosage form.

10 13. The method of Claim 12, wherein the dosage form releases the prodrug gradually over a period of at least about 6 hours after swallowing the dosage form, thereby providing a therapeutic concentration of a GABA analog in the plasma of the patient.

15 14. The method of Claim 12, wherein the dosage form is an osmotic dosage form, a prodrug-releasing polymer, a prodrug-releasing lipid, a prodrug-releasing wax, tiny timed-release pills or prodrug releasing beads.

20 15. The method of Claim 1 or Claim 2, wherein the prodrug of a GABA analog has the structure of Formula (I):



or a pharmaceutically acceptable salt, hydrate or solvate thereof, wherein:

n is 0 or 1;

25 Y is O or S;

R¹⁶ is hydrogen, alkyl or substituted alkyl;

R² is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, substituted acyl, alkoxycarbonyl, substituted alkoxycarbonyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl,
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substituted cycloheteroalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, or optionally, R² and R¹⁶ together with the atoms to which they are attached form a cycloheteroalkyl or substituted cycloheteroalkyl ring;

5 R³ and R⁶ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl and substituted heteroarylalkyl;

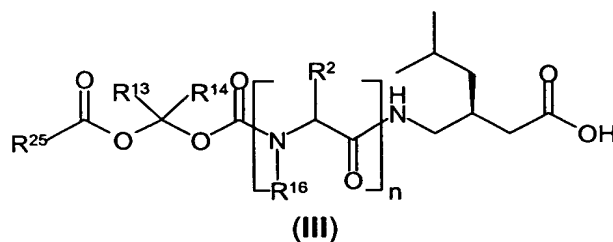
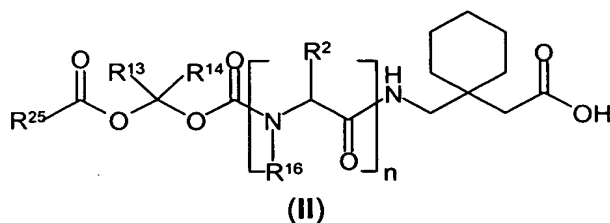
 R⁴ and R⁵ are independently selected from the group consisting of hydrogen,
10 alkyl, substituted alkyl, acyl, substituted acyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl and substituted heteroarylalkyl or optionally, R⁴ and R⁵ together with the carbon atom to which they are attached form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted
15 cycloheteroalkyl or bridged cycloalkyl ring;

 R⁷ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl and substituted
20 heteroarylalkyl;

 R¹³ and R¹⁴ are each independently hydrogen, alkyl, substituted alkyl, alkoxycarbonyl, substituted alkoxycarbonyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, carbamoyl, substituted carbamoyl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl or substituted
25 heteroarylalkyl or optionally, R¹³ and R¹⁴ together with the carbon atom to which they are attached form a cycloalkyl, substituted cycloalkyl, cycloheteroalkyl or substituted cycloheteroalkyl ring; and

 R²⁵ is selected from the group consisting of acyl, substituted acyl, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, cycloalkyl,
30 substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, heteroalkyl, substituted heteroalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl and substituted heteroarylalkyl.

16. The method of Claim 15, wherein the prodrug of a GABA analog has the structure of Formulae (II) or (III):



17. The method of Claim 16, wherein n is 0.

18. The method of Claim 16, wherein n is 1, R¹⁶ is hydrogen and R² is selected from the group consisting of hydrogen, methyl, 2-propyl, 2-butyl, isobutyl, *tert*-butyl, cyclopentyl, cyclohexyl, phenyl, benzyl, 4-hydroxybenzyl, 4-imidazolylmethyl, 3-indolylmethyl, -CH₂OH, -CH(OH)CH₃, -CH₂CO₂H, -CH₂CH₂CO₂H, -CH₂CONH₂, -CH₂CH₂CONH₂, -CH₂CH₂SCH₃, -CH₂SH, -CH₂(CH₂)₃NH₂ and -CH₂CH₂CH₂NHC(NH)NH₂.

19. The method of Claim 17, wherein R²⁵ is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl and *sec*-butyl, R¹³ is methyl and R¹⁴ is hydrogen.

20. The method of Claim 17, wherein R²⁵ is isopropyl, R¹³ is methyl and R¹⁴ is hydrogen.

21. A pharmaceutical composition for treating a patient suffering from hot flashes comprising a therapeutically effective amount of a prodrug of a GABA analog or a pharmaceutically acceptable salt, hydrate or solvate thereof, and a pharmaceutically acceptable vehicle.

22. A pharmaceutical composition for preventing hot flashes in a patient at risk of hot flashes comprising a therapeutically effective amount of a prodrug of a GABA analog or a pharmaceutically acceptable salt, hydrate or solvate thereof and a pharmaceutically acceptable vehicle.
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